

Hepatitis C virus genotype distribution in Ordu province

HCV genotype distribution in Ordu

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Abstract

Aim: It is important to increase the number of studies on genotype distributions from different centers and regions of the country in terms of identifying the HCV genotype distribution in the whole country in general and creating appropriate treatment algorithms. Our study aimed to identify the HCV genotype distribution in patients infected with HCV attending our hospital in Ordu Province in the Central Black Sea region. **Material and Method:** The study included a total of 196 patients whose samples were sent to our laboratory for HCV viral load measurements from January 2016 to May 2018 with HCV-RNA positivity identified. Genotype definition was completed with the real-time PCR method. **Results:** It was observed that 4 patients (2%) had genotype 1, 7 patients (3.6%) had genotype 1a, 179 patients (91.4%) had genotype 1b, 5 patients (2.5%) had genotype 3 and 1 patient (0.5%) had genotype 4. **Discussion:** The most common genotype observed among patients attending our hospital was genotype 1. Genotypes 3 and 4 were rarely observed in comparison to Turkish data, similar to other provinces in regions receiving little migration. As medication resistance and treatment failure is high for genotype 1, the risk of encountering treatment failure continues to be a serious problem in our region.

Keywords

Hepatitis C Virus; HCV RNA; HCV Genotypes

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Introduction

Hepatitis C virus (HCV) infection is a significant global health problem. The World Health Organization estimates more than 170 million people are chronic carriers of HCV [1]. HCV infections may cause chronic hepatitis, liver cirrhosis and hepatocellular carcinoma [2]. HCV is an enveloped and single-stranded RNA virus from the Flaviviridae family [3]. The virus shows rapid replication and RNA transcription errors occurring during this process play an important role in chronic development of infections. Viral assemblages forming as a result of these errors, form HCV genotypes [4]. There are seven genotypes and 67 subtypes identified for HCV [5]. In Turkey, genotype 1b is observed most commonly, with treatment response at lower levels for genotype 1b compared to other genotypes [6-11].

It is important to increase the number of studies on genotype distributions from different centers and regions of the country in terms of identifying the HCV genotype distribution in the whole country in general and creating appropriate treatment algorithms. In this study, we aimed to identify HCV genotype profiles for HCV-RNA positive serum samples obtained from blood samples of patients with chronic hepatitis C (CHC) diagnosis in Ordu province and thus to contribute to regional molecular epidemiology data.

Material and Method

Patient serum samples sent to Ordu Education and Research Hospital molecular microbiology laboratory from January 2016 to May 2018 for HCV viral load measurement and positive for CHC were included in the assessment. The demographic data like age and sex of the patients were recorded. Quantitative HCV-RNA real-time PCR tests were completed using a COBAS AmpliPrep/COBAS Taqman 48 system (Roche, Branchburg, NJ, USA). In determining HCV genotype, Bosphore HCV genotype (Anatolia Geneworks, Türkiye) real-time PCR method was used according to the manufacturer's instructions.

Results

The study included 196 patients with HCV-RNA positivity. Of all patients, 116 were female (59%) and 80 were male (41%). Mean age of the patients was 65 years (age interval 20-90).

Twenty-three patients (11.7%) were in the 20-50 age group, with the remaining 173 (88.3%) above the age of 50. It was observed that 4 patients (2%) had genotype 1, 7 patients (3.6%) had genotype 1a, 179 patients (91.4%) had genotype 1b, 5 patients (2.5%) had genotype 3 and 1 patient (0.5%) had genotype 4. The genotype distribution according to sex is shown in Table 1. Two of the three patients who were foreign nationals had genotype 1b and one had genotype 3.

Discussion

Determination of HCV genotype is an important parameter determining the antiviral treatment duration and response for CHC patients. HCV genotypes display epidemiologic differences between each other. The geographic distributions in the target group vary. Genotype 3a is observed among intravenous drug users in northern Europe, while 4a is mainly observed in the Middle East and genotype 1b, 2a and 2b infections are observed in elderly populations in Europe and Asia and linked to blood transfusions [12]. Harman et al. in a study of 160 patients identified the mean age as 56 years and reported 25% of patients were in the 18-50 year group while 75% were above the age of 50 [10]. In our study, the mean age was identified as 65 years and 88.3% of patients were in the over 50 age group. Additionally, 59% of CHC cases in our study were female. Similarly, there are studies showing the prevalence of HCV infection in our country is higher for women compared to men for all age groups [13].

Genotype investigations, which direct treatment and provide important epidemiologic data, identified that genotype 1 was most commonly observed in Turkey. Phylogenetic analysis of

Table 1. HCV genotype distributions by gender and mean age.

HCV Genotypes	Mean Age	Female/Male	Total (n(%))
Type 1	73.3	2/2	4 (2)
Type 1a	53.8	3/4	7 (3.6)
Type 1b	65.8	108/71	179 (91.4)
Type 3	50	3/2	5 (2.5)
Type 4	54	-/1	1 (0.5)
Total	65	116/80	196 (100)

Table 2. HCV genotype distribution from various cities in Turkey

Study	Year	Region	n	HCV genotype (%)										
				1	1a	1b	2	2b	3	3a	4	4a	5a	6
Aktas (6)	2010	Western Black Sea	39	-	2.6	97.4	-	-	-	-	-	-	-	-
Akgun (7)	2017	Adiyaman	71	4.22	8.45	71.83	-	11.27	-	4.22	-	-	-	
Ozturk (8)	2014	Antakya	324	-	0.31	86.73	9.26	-	0.93	-	2.78	-	-	
Ozturk (8)	2014	Adana	315	-	3.49	55.24	14.6	-	26.03	-	0.63	-	-	
Ural (9)	2007	Konya	80	-	-	100	-	-	-	-	-	-	-	
Harman (10)	2017	Gaziantep	160	98	-	-	0.75	-	1.25	-	-	-	-	
Tüzüner (11)	2018	Konya	480	2.9	3.5	82.6	1.7	1.3	0.2	3.1	1.9	0.6	0.2	
Çetin Duran (15)	2017	Adana	119	-	12.6	58.8	7.6	-	16.8	-	3.4	-	-	
Buruk (16)	2013	Eastern Black Sea	304	-	5.3	87.5	1.6	-	4.9	-	0.7	-	-	
Gökahmetoğlu (17)	2011	Kayseri	146	61.7	-	-	2.7	-	-	-	35.6	-	-	
Sarıgülzel (18)	2015	Kayseri	100	70	-	-	4	-	2	-	24	-	-	
Kirişçi (19)	2013	Kahramanmaraş	100	60	-	-	40	-	-	-	-	-	-	
This study	2018	Ordu	196	2	3.6	91.4	-	-	2.5	-	0.5	-	-	

genotype 1 considered it came from Greece in the 1900s and spread to Cyprus and Turkey in the 1920-1930s and spread from 1940-1999 due to unsafe interventions and instruments [14].

The most common subtype of genotype 1 commonly observed in Turkey is genotype 1b (Table 2). A study in Adana with 119 patients identified 71.4% had genotype 1 (12.6% genotype 1a, 58.8% genotype 1b), 16.8% genotype 3, 7.6% genotype 2 and 3.4% genotype 4 infection. Additionally, a Syrian female patient was found to have genotype 5a (0.8%) previously not reported from Adana [15]. A study in Gaziantep included a total of 160 patients, and identified only one patient with HCV genotype 2 and two patients with genotype 2 with the remaining 157 patients (98%) identified to have genotype 1b [10]. A total of 480 patients from a study in Konya found 396 (82.6%) genotype 1b, 17 (3.5%) genotype 1a, 15 (3.1%) genotype 3a, 14 (2.9%) genotype 1, 9 (1.9%) genotype 4, 8 (1.7%) genotype 2, 6 (1.3%) genotype 2b, 5 (1.0%) genotype 1a/1b, 4 (0.8%) genotype 2a/2c, 3 (0.6%) genotype 4a, and 1 each (0.2%) for genotype 3, genotype 5a and genotype 6 [11]. A study including 304 patients from Eastern Black Sea provinces (Artvin, Bayburt, Giresun, Gümüşhane, Rize, and Trabzon) found varying rates of four genotypes (1, 2, 3 and 4) with the dominant genotype 1 (92.8%) and dominant subtype 1b (87.5%). The prevalence of HCV subtype 1a, genotypes 2, 3 and 4 were 5.3%, 1.6%, 4.9% and 0.7%, respectively. Additionally, the study observed that Giresun, Gümüşhane and Bayburt provinces with relatively low immigration had high levels of HCV genotype 1, while data belonging to Trabzon, Rize, and Artvin was affected by higher settlement by foreign nationals [16]. Similar to this data, in our study genotype 1b was the most commonly identified genotype in 91.4% of the study group. One of the five patients with genotype 3 and two of the 179 patients with genotype 1b were found to be foreign nationals.

Due to increasing intravenous drug use in Turkey, there is an increase in other genotypes, led by genotype 3. In some centers, genotype 3 and 4 cases comprise 1/3 of total cases. In Kayseri, more than one-third of genotypes were reported to be genotype 4 [17]. The phylogenetic analysis showed that HCV genotype 4d samples in this region were in 82 - 95% similarity with genotype 4d strains of different geographical regions. Genotype 4d strains are thought to have come to this region 30 - 75 years ago according to molecular clock analysis [18]. In Kahramanmaraş, up to 40% prevalence of genotype 3 was identified and this was among young people with drug abuse held responsible [19]. Another study from Adana including 87 intravenous drug users identified 58.6% genotype 3, 29.9% genotype 2 and 11.5% genotype 1 [20]. In our study, genotype 3 and 4 were 2.5% and 0.5%, respectively.

In conclusion, this is the first study showing HCV genotype distribution in Ordu province. The results are similar to other studies from Turkey, with genotype 1 which is the most common among CHC patients attending our hospital. The distribution of genotypes 3 and 4 were low compared to Konya and Kayseri, and similar to other provinces receiving little migration like Giresun, Gümüşhane and Bayburt. As drug resistance and treatment failure is high in genotype 1 and genotype 4, the risk of encountering treatment failure continues to be a serious

problem in our region. HCV genotype definition is necessary to being treatment for HCV infections in Turkey and to determine treatment protocols. Determination of the molecular epidemiology of HCV and monitoring the genotype profile is important considering all these characteristics.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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